CASE REPORTS

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Wegener Granulomatosis With Avascular Necrosis of a Lower Extremity

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WEGENER* GRANULOMATOSIS with its common presentation of the generalized form involving upper and lower airways, as well as the kidneys, is diagnosed by its histologic hallmark of necrotizing granulomatous vasculitis. This has been a uniformly lethal disease since the first three cases reported by Wegener in 1936[1,2] until the early 1960's when maximal survival time was approximately five months. During the 1960's beneficial effects of corticosteroid therapy as well as therapy with various cytotoxic agents, either used alone or in combination with corticosteroids, were reported in the literature.

More recently, significant therapeutic responses have been reported in two studies of long-term follow-up of patients treated with cyclophosphamide.[3,4]

The following is a case report of Wegener granulomatosis with an unusual complication as illustrated by accompanying illustrations.

Report of a Case

A 62-year-old white man was admitted to the hospital in October 1975 because of a sudden loss of vision in his left eye. He was well until two months previously when symptoms of an upper respiratory infection developed. A few weeks later, he presented with maxillary sinusitis which required drainage and appropriate antibiotic therapy (Enterobacter sp) as an inpatient.

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*The WESTERN JOURNAL's style regarding eponyms is that they are not written in the possessive form; therefore, Graves disease, Ewing sarcoma and Paget disease. An explanation may be found on page 78 of the July 1978 issue.

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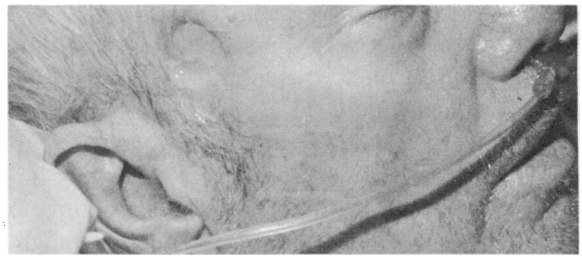

Figure 1.—Spontaneous, draining ulcerations on scalp.

After the patient left the hospital, the vision in his left eye deteriorated rapidly, although an ophthalmological examination showed no abnormalities. X-ray studies of the skull showed a destructive process of the left lesser wing of the sphenoid bone along the superior margin of the superior orbital fissure and the patient was readmitted for further studies.

On physical examination, he appeared alert and oriented but almost completely deaf, having the ability to hear only loud sounds very close to his right ear. Body temperature ranged between 37.2° and 38.3°C (99° and 101°F). Pulse was 130 beats per minute and regular, and respirations 30 per minute. Blood pressure was 120/70 mm of mercury.

There were multiple draining skin lesions on the scalp and left leg (Figure 1), and also tender, purple, subcutaneous nodules in both legs. The left pupil was fixed and nonreactive to light with impairment of ocular movement and lid ptosis. The left tympanic membrane was opaque and yellowish. The nasal mucosa was dry with scanty dried secretions. Pressure over the maxillary and frontal sinuses did not elicit tenderness. The throat was clear, without ulcerations or exudates and the palate was intact. No lymph node enlargement was present.

Mild expiratory wheezes were present on lung auscultation. The heart was normal except for tachycardia. Findings on abdominal examination were normal.

Neurological examination disclosed left third cranial nerve palsy as described above and testing of the eighth cranial nerve showed intact bone conduction and decreased air conduction. Sensation in both feet was diminished in a "stocking

pattern." The peripheral pulses were symmetrical and strong except the dorsalis pedis which were not palpable bilaterally.

The blood count showed a hemoglobin of 10.9 grams per dl with a hematocrit of 44.9 percent. Leukocyte count was 13,800 per cu mm, and the platelets were reported to be normal to slightly increased. Analysis of urine showed 20 to 25 red blood cells per high-power field. The serum alkaline phosphatase value was 240 mU per ml (normal limits 30 to 85 mU per ml). The erythrocyte sedimentation rate (by Westergren method) was 90 mm per hour (it had been 30 mm per hour two weeks earlier).

X-ray studies of the skull showed severe demineralization and osteolytic destruction of the superior wing of the left optic foramen and left lesser wing of sphenoid and also along the superior margin of the superior orbital fissure. Results of a brain scan were normal. A bone scan showed increased uptake in the left facial bones. An x-ray study of the chest showed infiltrates which developed bilaterally in the interval since the last admission. A lung scan showed bilateral multiple defects suggestive of either pulmonary emboli or bronchopneumonia.

Consultation with an ear, nose and throat specialist established that a nasal septum perforation took place in the two week interval since the patient's previous admission. Biopsy specimens were taken from the nasal septum and ethmoid bone as well as from subcutaneous nodules and skin ulcerations. The microscopic lesions of necrotizing vasculitis and granulomata were present in all specimens (Figures 2, 3 and 4).

On the seventh day after admission, tachycardia developed and the patient became increasingly dyspneic. Studies of arterial blood gases showed hypoxia, increase in the alveolar-arterial gradient and uncompensated metabolic acidosis. An electrocardiogram showed arrhythmias: transient bige-

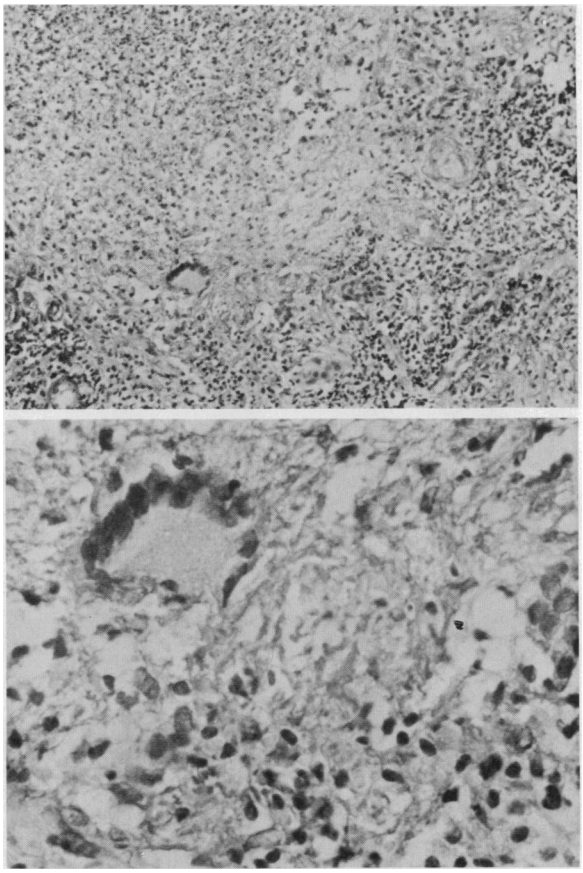

Figure 2.—Top, Necrotizing granuloma in ethmoid bone biopsy (reduced from 100×). **Bottom.** Necrotizing granuloma in ethmoid (reduced from 400×).

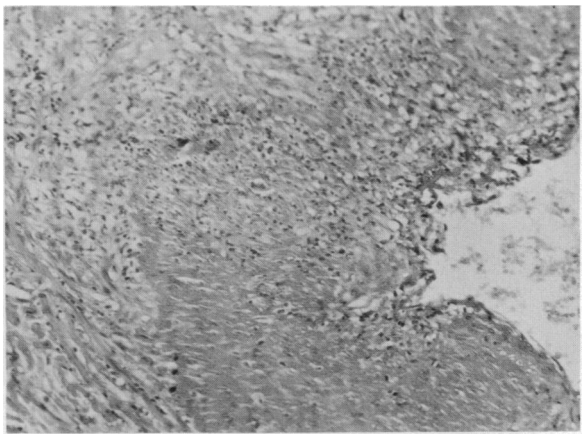

Figure 3.—Inflammatory granulation tissue in subcutaneous lesion of right leg (reduced from 40×).

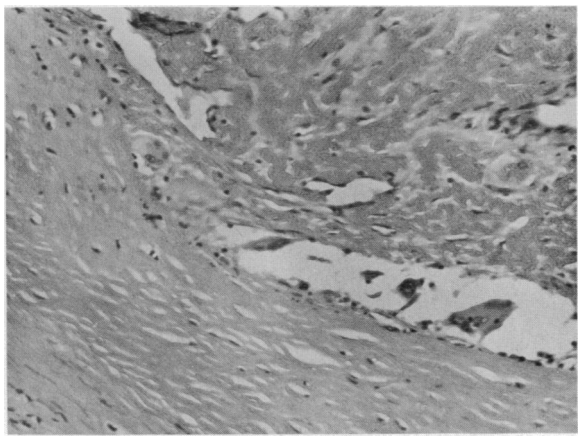

Figure 4.—Necrotizing inflammation with presence of giant cells in subcutaneous blood vessel; organizing thrombosis in this vessel can be seen.

miny, wandering atrial pacemaker and eventually atrial fibrillation with venticular rate of 120 per minute. The patient was transferred to the intensive care unit and his condition monitored. On the eighth day after admission, the clinical suspicion of Wegener granulomatosis was confirmed and the treatment with cyclophosphamide at a dose of 125 mg per day given orally was started. An x-ray film of the chest showed development of bilateral infiltrates and the red blood cells in the urine sediment increased to 150 to 175 per high-power field. The leukocyte count was 14,000 per cu mm, and the platelet count was 715,000 per cu mm. On the tenth day after admission, pain developed suddenly in the patient's left foot with cyanosis and decreased capillary filling. The pulse of the left posterior tibial artery was not palpable. At the same time as the apparent embolic incident, numerous new subcutaneous nodules appeared on the lower left leg. An embolectomy was carried out the next day, but restoration of arterial circulation was not achieved.

In view of the deterioration of the clinical condition as expressed by extension of lung infiltrates, increase of number of red blood cells in the urine sediment and decrease of the creatinine clearance from 114 ml per minute to 70 ml per minute, the cyclophosphamide therapy was continued with a daily dose of 200 mg given intravenously.

On the 18th day, the left leg was amputated below the knee. Pathological examination gave the following findings: (1) Occlusive arteriosclerosis of peripheral vessels with organizing thrombus of the left anterior tibial artery, (2) granulomatous vasculitis with necrosis in adjacent muscle tissue (Figures 3 and 4) and (3) ulcer of leg (Figure 5).

The postoperative course was satisfactory. After eight days of intravenous administration, cyclophosphamide was continued orally at a daily dose of 125 mg (1.5 mg per kg of body weight).

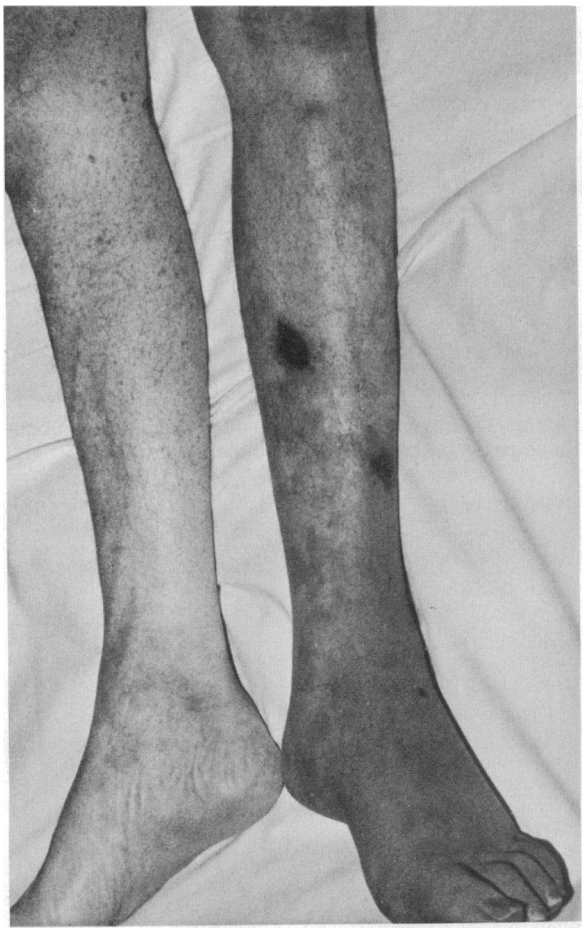

Figure 5.—Subcutaneous nodules, one of them spontaneously ulcerated on leg (impaired circulation reflected by cyanosis).

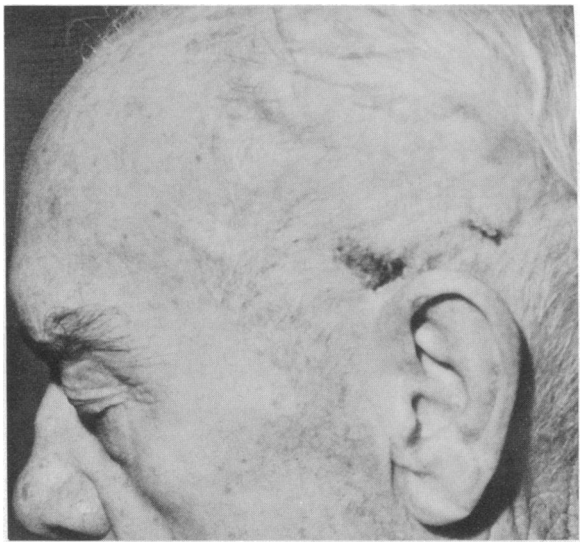

Figure 6.—Healing scalp ulceration after treatment; "saddle nose" due to septal perforations can be seen.

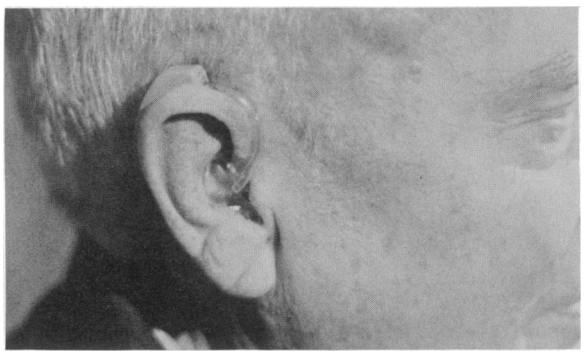

Figure 7.—Patient shown one year after treatment.

There was pronounced clinical improvement as assessed by the following: (1) clearing of lung infiltrates, (2) spontaneous conversion to sinus rhythm, (3) decrease of number of red blood cells in urine sediment and (4) improvement of creatinine clearance to normal.

The patient was discharged from the hospital after being in the rehabilitation unit, where he received extensive physical and occupational therapy (Figure 6). He has since been in remission and continues to receive 125 mg cytoxan orally per day. The leukocyte count is stable above 3,000 per cu mm, and the platelets eventually returned to the normal range. A prosthetic device for the left leg and use of a hearing aid has made it possible for the patient to resume daily activities. (See Figure 7.)

The arrhythmia that preceded the embolic episode in this case was very likely due to vasculitic involvement of coronary vessels; such occurrences have been reported in the literature.[5] The spontaneous conversion to sinus rhythm along with improvement of respiratory and renal findings on cyclosphosamide therapy seems to confirm this assumption. We also feel that the extensive vasculitic involvement was responsible for the inability to maintain a viable leg due to ineffective collateral circulation.

Summary

A case of generalized Wegener granulomatosis has been presented with typical multisystem involvement including the respiratory tract, kidneys, skin, cranial nerves, heart and hematopoietic system. In addition, a heretofore unreported complication has also been presented, namely avascular necrosis of an extremity, requiring amputation. "Pulseless disease" and avascular necrosis after embolectomy should alert physicians to extensive involvement of collaterals by a vasculitic process.

While the classification and causes of this interesting disorder still remain elusive, the introduction of cyclophosphamide has at least offered a much brighter perspective for improvement and possible cure.[3,4]

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Refer to: Warick LH: Lithium poisoning—Report of a case with neurologic, cardiac and hepatic sequelae. West J Med 130:259-263, Mar 1979

Lithium Poisoning

Report of a Case With Neurologic, Cardiac and Hepatic Sequelae

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LITHIUM CARBONATE is now a well established agent for the treatment of acute mania and for prophylaxis in patients with recurrent manic and depressive bipolar as well as a number of unipolar recurrent episodes.[1,2] The treatment of manic-depressive patients with this agent, its dosage, monitoring schedules, therapeutic blood levels and narrow therapeutic-toxic range have been outlined by Schou[1] and other authors.[3,4]

Lithium toxicity is closely related to serum lithium levels and can occur at doses close to therapeutic levels (see discussion).

Lithium therapy requires extreme caution and thorough knowledge by physicians in situations when patients are on severe diets or have low sodium intake; in cases of heavy fluid loss (diarrhea, vomiting or fever) or cardiac-renal problems; in aging patients with decreased renal clearance, and in schizophrenic and depressive patients, whose tolerance for lithium is lower than that of manic patients.[1,5]

Historically, the use of lithium salts as a substitute for sodium chloride in patients with cardiac disease gave rise to early reports on the neurotoxicity of lithium ions.[6,7]

The clinical manifestations of lithium intoxication have been well documented by Schou.[8] In general, patients have either died or completely recovered, with no lasting neurologic sequelae. Recent evidence indicates, however, that permanent neurologic[9] or cardiac or hepatic damage can result from lithium intoxication. This communication will present such evidence.

Report of a Case

A 36-year-old businessman with a severely obtunded sensorium and with coarse tremors of his extremities was brought into the emergency

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